

SEQUENCE LISTING

<110> Glotzer, Michael Jantsch-Plunger, Verena Romano, Alper Mishima, Masanori Kaitna, Susanne <120> Cyk-4 polypeptides, DNA molecules encoding them and their use in screening methods <130> 0652.2260001/EKS/AES <140> US 09/881,736 <141> 2001-06-18 <150> EP 00 112 880.0 <151> 2000-06-19 <150> EP 01 110 554.1 <151> 2001-04-30 <150> 60/241,231 <151> 2000-10-18 <150> To be determined <151> 2001-06-13 <160> 8 <170> PatentIn Ver. 2.1 <210> 1 <211> 3050 <212> DNA <213> Homo sapiens <220> <221> 5'UTR <222> (1)..(70) <220> <221> CDS <222> (71)..(1969) <220> <221> 3'UTR <222> (1970)..(3050) <400> 1 taaagggggg tgccagacca ggtgcgtctg ccgctggatt gtgataggaa gcagagtgtt 60 cgtgtgaaag atg gat act atg atg ctg aat gtg cgg aat ctg ttt gag Met Asp Thr Met Met Leu Asn Val Arg Asn Leu Phe Glu

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Asp		His	_	Ile	tgt Cys	Ser	Leu		Lys	Āsp		Leu	_			1357
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His Glu Leu Gly Lys Tyr Lys Asp Leu Leu Met Lys Ala Glu Thr Glu
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Arg Ser Ala Leu Asp Val Lys Leu Lys His Ala Arg Asn Gln Val Asp 65 70 75 80

Val Glu Ile Lys Arg Arg Gln Arg Ala Glu Ala Asp Cys Glu Lys Leu 85 90 95

Glu Arg Gln Ile Gln Leu Ile Arg Glu Met Leu Met Cys Asp Thr Ser 100 105 110

Gly Ser Ile Gln Leu Ser Glu Glu Gln Lys Ser Ala Leu Ala Phe Leu 115 120 125

Asn Arg Gly Gln Pro Ser Ser Ser Asn Ala Gly Asn Lys Arg Leu Ser 130 135 140

Thr Ile Asp Glu Ser Gly Ser Ile Leu Ser Asp Ile Ser Phe Asp Lys
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Thr Asp Glu Ser Leu Asp Trp Asp Ser Ser Leu Val Lys Thr Phe Lys 165 170 175

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Gly Pro Pro Gly Pro Val Lys Lys Thr Arg Ser Ile Gly Ser Ala Val 195 200 205

Asp Gln Gly Asn Glu Ser Ile Val Ala Lys Thr Thr Val Thr Val Pro 210 215 220

Asn Asp Gly Gly Pro Ile Glu Ala Val Ser Thr Ile Glu Thr Val Pro

225 230 235 240 Tyr Trp Thr Arg Ser Arg Arg Lys Thr Gly Thr Leu Gln Pro Trp Asn 245 Ser Asp Ser Thr Leu Asn Ser Arg Gln Leu Glu Pro Arg Thr Glu Thr 265 Asp Ser Val Gly Thr Pro Gln Ser Asn Gly Gly Met Arg Leu His Asp Phe Val Ser Lys Thr Val Ile Lys Pro Glu Ser Cys Val Pro Cys Gly 295 Lys Arg Ile Lys Phe Gly Lys Leu Ser Leu Lys Cys Arg Asp Cys Arg Val Val Ser His Pro Glu Cys Arg Asp Arg Cys Pro Leu Pro Cys Ile 330 Pro Thr Leu Ile Gly Thr Pro Val Lys Ile Gly Glu Gly Met Leu Ala 345 Asp Phe Val Ser Gln Thr Ser Pro Met Ile Pro Ser Ile Val Val His 360 Cys Val Asn Glu Ile Glu Gln Arg Gly Leu Thr Glu Thr Gly Leu Tyr 375 Arg Ile Ser Gly Cys Asp Arg Thr Val Lys Glu Leu Lys Glu Lys Phe Leu Arg Val Lys Thr Val Pro Leu Leu Ser Lys Val Asp Asp Ile His 405 Ala Ile Cys Ser Leu Leu Lys Asp Phe Leu Arg Asn Leu Lys Glu Pro Leu Leu Thr Phe Arg Leu Asn Arg Ala Phe Met Glu Ala Ala Glu Ile Thr Asp Glu Asp Asn Ser Ile Ala Ala Met Tyr Gln Ala Val Gly Glu 455 Leu Pro Gln Ala Asn Arg Asp Thr Leu Ala Phe Leu Met Ile His Leu 475 Gln Arg Val Ala Gln Ser Pro His Thr Lys Met Asp Val Ala Asn Leu Ala Lys Val Phe Gly Pro Thr Ile Val Ala His Ala Val Pro Asn Pro 505 Asp Pro Val Thr Met Ser Gln Asp Ile Lys Arg Gln Pro Lys Val Val Glu Arg Leu Leu Ser Leu Pro Leu Glu Tyr Trp Ser Gln Phe Met Met 535 Val Glu Gln Glu Asn Ile Asp Pro Leu His Val Ile Glu Asn Ser Asn 545 550

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Tyr Gln Arg Thr Asn Gln Glu Leu Glu Lys Phe Lys Asp Leu Leu

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Lys Ala Glu Thr Gly Arg Ser Ala Leu Asp Val Lys Leu Lys His Ala

362

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560 565 570

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Arg Leu Val Ser His Pro Glu Cys Arg Asp Arg Cys Pro Leu Pro Cys

Ile Pro Pro Leu Val Gly Thr Pro Val Lys Ile Gly Glu Gly Met Leu

340 345 350

Ala Asp Phe Val Ser Gln Ala Ser Pro Met Ile Pro Ala Ile Val Val 355 360 365

Ser Cys Val Asn Glu Ile Glu Gln Arg Gly Leu Thr Glu Ala Gly Leu 370 380

Tyr Arg Ile Ser Gly Cys Asp Arg Thr Val Lys Glu Leu Lys Glu Lys 385 390 395 400

Phe Leu Lys Val Lys Thr Val Pro Leu Leu Ser Lys Val Asp Asp Ile 405 410 415

His Val Ile Cys Ser Leu Leu Lys Asp Phe Leu Arg Asn Leu Lys Glu 420 425 430

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Leu Gln Arg Val Ser Gln Ser Pro Asp Thr Lys Met Asp Ile Ala Asn
485 490 495

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Pro Asp Pro Val Thr Met Phe Gln Asp Ile Lys Arg Gln Leu Lys Val 515 520 525

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Thr Pro Arg Thr Pro Asp Val Lys Val Ser Leu Leu Gly Pro Val Thr 565 570 575

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200

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Lys Leu Trp Lys Asp Ser Glu Glu Ser Lys Lys Arg Leu Asn Ala Asp 50 55 60

Met Arg Glu Ala Glu Glu Ala Leu Ala Lys Ala Arg Lys Lys Leu Ala 65 70 75 80

Met Phe Asp Ile Asp Val Lys Asp Thr Gln Lys His Leu Arg Ala Leu 85 90 95

Met Glu Glu Asn Lys Ala Leu Lys Leu Asp Leu Asn Val Tyr Glu Thr 100 105 110

Arg Glu Lys Gln Leu Lys Asp Ala Met Lys Asn Gly Ile Phe Asn Ser 115 120 125

Leu Thr Lys Glu Asp Arg Asp Gln Phe Lys Phe Leu His Glu Pro Leu 130 135 140

Val Arg Thr Tyr Ser Lys Arg Val Gln Gln Arg His Pro His Leu Met 145 150 155 160

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Thr Gly Asp Ser Phe Glu Glu Val Ile His Leu Arg Asn Gly Arg Glu 180 185 190

Val Arg Arg Ser Ser Ala Ala Gly Asn Ala Val Gly Gly Lys Arg Arg 195 200 205

Ser Ala Ser Ala His Ala Ile Thr Ala Ala Ala Asn Ser Lys Arg Ser 210 215 220

Arg Ser Arg Val Met Thr Ala Thr Ile Asp Glu Glu Pro Asn Glu Gly 225 230 235 240

Gly Thr Pro Pro Lys Arg Cys Arg Asp Asp Gly Ser Thr Pro His Gln 245 250 255

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- Thr Pro Gly Gln Thr Thr Asn Asn Ile Gly Leu Gly Met Ser Ser Ala 305 310 315 320
- Ile Leu Thr Lys Ser Thr Leu Asp Ile Arg Thr Leu Lys Arg Gly Thr 325 330 335
- Pro Ala Trp Thr Asn Gly Thr Thr Arg Asp Ile Ala Met Arg Pro His 340 345 350
- Thr Phe Ile Glu Ala Gly Ile Lys Ala Met Arg Lys Cys Asp Lys Cys 355 360 365
- Ala Thr Ala Leu Lys Leu Ala Thr Ser Met Lys Cys Arg Asp Cys His 370 380
- Gln Val Val His Arg Ser Cys Cys Asn Lys Leu His Leu Pro Cys Ile 385 390 395 400
- Pro Arg Pro Lys Thr Met Met Thr Pro Lys Ser Ala Leu Arg Gly Ala 405 410 415
- Lys Pro Gly Ala Gly Glu Phe Arg Leu Gln Asp Leu Cys Thr Ser Ala 420 425 430
- Lys Pro Met Ile Pro Ala Ala Val Ile His Cys Val Val Ala Leu Glu 435 440 445
- Ala Arg Gly Leu Thr Gln Glu Gly Ile Tyr Arg Val Pro Gly Gln Val 450 455 460
- Arg Thr Val Asn Val Leu Leu Asp Glu Leu Arg Ser Lys Thr Val Pro 465 470 475 480
- Asn Val Gly Leu His Asp Val Glu Val Ile Thr Asp Thr Leu Lys Arg 485 490 495
- Phe Leu Arg Asp Leu Lys Asp Pro Leu Ile Pro Arg Thr Ser Arg Gln 500 505 510
- Glu Leu Ile Val Ala Ala Asn Leu Tyr Ser Thr Asp Pro Asp Asn Gly
 515 520 525
- Arg Leu Ala Leu Asn Arg Val Ile Cys Glu Leu Pro Gln Ala Asn Arg 530 535 540
- Asp Thr Leu Ala Tyr Leu Phe Ile His Trp Arg Lys Val Ile Ala Gln 545 550 555
- Ser Ser Arg Asn Lys Met Asn Cys Glu Ala Met Ala Arg Met Val Ala 565 570 575
- Pro Ala Val Met Gly His Pro Val Lys Gln Ser Gln Ser Gln Ala Ile 580 585 590
- Ala Gly Arg Asp Ala Thr Asp Cys His Arg Ala Met Thr Ala Leu Phe 595 600 605
- Glu Phe Asp Asp Val Tyr Trp Gln Arg Phe Leu Gly Thr Ser Ala Val

610 615 620

Ser Met Ala Ser Asn Gln Ile Glu Thr Ala Arg His Gln Asp Asn Phe 625 630 635 640

Ala Leu Cys Asp Arg Ser Ile Leu Gly Pro Val Thr Thr Ser Pro Ala 645 650 655

Thr Pro Leu Leu Ala Arg Ser Ala Asn Ala Thr Arg Ala Arg Gly Ala 660 665 670

His Leu Leu Gly Ser Met Phe His Asp 675 680

<210> 7

<211> 772

<212> PRT

<213> Caenorhabditis elegans

<400> 7

Met Ser Ser Arg Lys Arg Gly Ile Thr Pro Ser Arg Asp Gln Val Arg 1 $$ 5 $$ 10 $$ 15

Arg Lys Lys Leu Ser Ile Glu Glu Thr Asp Ser Ile Glu Val Cys
20 25 30

Arg Leu Cys Pro Tyr Thr Gly Ser Thr Pro Ser Leu Ile Ala Ile Asp 35 40 45

Glu Gly Ser Ile Gln Thr Val Leu Pro Pro Ala Gln Phe Arg Arg Glu 50 55 60

Asn Ala Pro Gln Val Glu Lys Val Phe Arg Phe Gly Arg Val Phe Ser 70 75 80

Glu Asn Asp Gly Gln Ala Thr Val Phe Glu Arg Thr Ser Val Asp Leu 85 90 95

Ile Leu Asn Leu Leu Lys Gly Gln Asn Ser Leu Leu Phe Thr Tyr Gly
100 105 110

Val Thr Gly Ser Gly Lys Thr Tyr Thr Met Thr Gly Lys Pro Thr Glu 115 120 125

Thr Gly Thr Gly Leu Leu Pro Arg Thr Leu Asp Val Ile Phe Asn Ser 130 135 140

Ile Asn Asn Arg Val Glu Lys Cys Ile Phe Tyr Pro Ser Ala Leu Asn 145 150 155 160 Thr Phe Glu Ile Arg Ala Thr Leu Asp Ala His Leu Lys Arg His Gln 165 170 175

Met Ala Ala Asp Arg Leu Ser Thr Ser Arg Glu Ile Thr Asp Arg Tyr 180 185 190

Cys Glu Ala Ile Lys Leu Ser Gly Tyr Asn Asp Asp Met Val Cys Ser 195 200 205

Val Phe Val Thr Tyr Val Glu Ile Tyr Asn Asn Tyr Cys Tyr Asp Leu 210 215 220

Leu Glu Asp Ala Arg Asn Gly Val Leu Thr Lys Arg Glu Ile Arg His 225 230 235 240

Asp Arg Gln Gln Met Tyr Val Asp Gly Ala Lys Asp Val Glu Val
245 250 255

Ser Ser Ser Glu Glu Ala Leu Glu Val Phe Cys Leu Gly Glu Glu Arg
260 265 270

Arg Arg Val Ser Ser Thr Leu Leu Asn Lys Asp Ser Ser Arg Ser His
275 280 285

Ser Val Phe Thr Ile Lys Leu Val Met Ala Pro Arg Ala Tyr Glu Thr 290 295 300

Lys Ser Val Tyr Pro Thr Met Asp Ser Ser Gln Ile Ile Val Ser Gln 305 310 315 320

Leu Cys Leu Val Asp Leu Ala Gly Ser Glu Arg Ala Lys Arg Thr Gln
325 330 335

Asn Val Gly Glu Arg Leu Ala Glu Ala Asn Ser Ile Asn Gln Ser Leu 340 345 350

Met Thr Leu Arg Gln Cys Ile Glu Val Leu Arg Arg Asn Gln Lys Ser 355 360 365

Ser Ser Gln Asn Leu Glu Gln Val Pro Tyr Arg Gln Ser Lys Leu Thr 370 375 380

His Leu Phe Lys Asn Tyr Leu Glu Gly Asn Gly Lys Ile Arg Met Val 385 390 395 400

- Ile Cys Val Asn Pro Lys Pro Asp Asp Tyr Asp Glu Asn Met Ser Ala 405 410 415
- Leu Ala Phe Ala Glu Glu Ser Gln Thr Ile Glu Val Lys Lys Gln Val 420 425 430
- Glu Arg Met Pro Ser Glu Arg Ile Pro His Ser Phe Phe Thr Gln Trp 435 440 445
- Asn Ser Glu Leu Asp Gly Ser Val Arg Met Glu Asp Asp Gly Ser Arg 450 455 460
- Glu Ile Pro Cys Pro Pro Thr Phe Cys Leu Thr Asp Cys Asn Asp Lys 465 470 475 480
- Asp Thr Val Asp Ser Met Tyr Lys Tyr Ala Arg Lys Leu Ser Ser Leu 485 490 495
- Gln Asn Ser Ser Glu Glu Gly Pro Ser Ser Thr Leu Leu Thr Met Ile 500 505 510
- Arg Gln Tyr Met Met Glu Ala Asp Tyr Gln Arg Val Glu Ile Ala Arg 515 520 525
- Leu Lys Asp Ser Leu Asn Asp Lys Asp Glu Glu Ile Lys Lys Leu Arg 530 535 540
- Gly Phe Cys Ser Arg Tyr Lys Arg Glu Asn Ala Ser Met Lys Glu Arg 545 550 555 560
- Ile Ala Ser Cys Glu Gl
n Gly Glu Gl
n Glu As
n Ala Leu Val Met Glu 565 570 575
- Lys Leu Met Glu Gln Lys Met Glu Asp Arg Lys Ile Ile Gln Ser Gln 580 585 590
- Lys Lys Ala Met Arg Asn Val Arg Gly Ile Ile Asp Asn Pro Ser Pro 595 600 605
- Ser Val Ala Ser Leu Arg Ser Arg Phe Asp Gln Glu Asn Val Ala His 610 615 620
- Pro Thr Ala Pro Ile Gln Thr Pro Pro Pro Pro Tyr Gln Thr Pro Gly 625 630 635 640

Arg Ala Pro Val Phe Lys Lys Arg Leu Glu Ala Thr Thr Ser Thr Thr 645 650 655

Val Met Ser Gly Ser Ser Ser Gly Gly Ser Gly Gln Gln Gly Tyr Val 660 665 670

Asn Pro Lys Tyr Gln Arg Arg Ser Lys Ser Ala Ser Arg Leu Leu Asp 675 680 685

His Gln Pro Leu His Arg Val Pro Thr Gly Thr Val Leu Gln Ser Arg 690 695 700

Thr Pro Ala Asn Ala Ile Arg Thr Thr Lys Pro Glu Met His Gln Leu 705 710 715 720

Asn Lys Ser Gly Glu Tyr Arg Leu Thr His Gln Glu Val Asp Asp Glu
725 730 735

Gly Asn Ile Ser Thr Asn Ile Val Lys Val Asn Ser Leu Val Ser Thr 740 745 750

Gln Lys His Ala Cys Thr Val Pro Leu Ser Phe Ser Arg Val Leu Ile 755 760 765

Thr His Leu Ser

<210> 8

<211> 856

<212> PRT

<213> Homo sapiens

<400> 8

Met Lys Ser Ala Arg Ala Lys Thr Pro Arg Lys Pro Thr Val Lys Lys 1 5 10 15

Gly Ser Gln Thr Asn Leu Lys Asp Pro Val Gly Val Tyr Cys Arg Val 20 25 30

Arg Pro Leu Gly Phe Pro Asp Gln Glu Cys Cys Ile Glu Val Ile Asn $35 \hspace{1cm} 40 \hspace{1cm} 45$

Asn Thr Thr Val Gln Leu His Thr Pro Glu Gly Tyr Arg Leu Asn Arg 50 55 60

Asn Gly Asp Tyr Lys Glu Thr Gln Tyr Ser Phe Lys Gln Val Phe Gly 65 70 75 80

Thr His Thr Thr Gln Lys Glu Leu Phe Asp Val Val Ala Asn Pro Leu 85 90 95

Val Asn Asp Leu Ile His Gly Lys Asn Gly Leu Leu Phe Thr Tyr Gly
100 105 110

Val Thr Gly Ser Gly Lys Thr His Thr Met Thr Gly Ser Pro Gly Glu 115 120 125

Gly Gly Leu Leu Pro Arg Cys Leu Asp Met Ile Phe Asn Ser Ile Gly 130 135 140

Ser Phe Gln Ala Lys Arg Tyr Val Phe Lys Ser Asn Asp Arg Asn Ser 145 150 155 160

Met Asp Ile Gln Cys Glu Val Asp Ala Leu Leu Glu Arg Gln Lys Arg 165 170 175

Glu Ala Met Pro Asn Pro Lys Thr Ser Ser Ser Lys Arg Gln Val Asp 180 185 190

Pro Glu Phe Ala Asp Met Ile Thr Val Glu Phe Cys Lys Ala Glu
195 200 205

Glu Val Asp Glu Asp Ser Val Tyr Gly Val Phe Val Ser Tyr Ile Glu 210 215 220

Ile Tyr Asn Asn Tyr Ile Tyr Asp Leu Leu Glu Glu Val Pro Phe Asp 225 230 235 240

Pro Ile Lys Pro Lys Pro Pro Gln Ser Lys Leu Leu Arg Glu Asp Lys 245 250 255

Asn His Asn Met Tyr Val Ala Gly Cys Thr Glu Val Glu Val Lys Ser 260 265 270

Thr Glu Glu Ala Phe Glu Val Phe Trp Arg Gly Gln Lys Lys Arg Arg 275 280 285

Ile Ala Asn Thr His Leu Asn Arg Glu Ser Ser Arg Ser His Ser Val 290 295 300

Phe Asn Ile Lys Leu Val Gln Ala Pro Leu Asp Ala Asp Gly Asp Asn 305 310 315 320

Val Leu Gln Glu Lys Glu Gln Ile Thr Ile Ser Gln Leu Ser Leu Val 325 330 335

Asp Leu Ala Gly Ser Glu Arg Thr Asn Arg Thr Arg Ala Glu Gly Asn 340 345 350

Arg Leu Arg Glu Ala Gly Asn Ile Asn Gln Ser Leu Met Thr Leu Arg 355 360 365

Thr Cys Met Asp Val Leu Arg Glu Asn Gln Met Tyr Gly Thr Asn Lys 370 375 380

Met Val Pro Tyr Arg Asp Ser Lys Leu Thr His Leu Phe Lys Asn Tyr 385 390 395 400

Phe Asp Gly Glu Gly Lys Val Arg Met Ile Val Cys Val Asn Pro Lys 405 410 415

Ala Glu Asp Tyr Glu Glu Asn Leu Gln Val Met Arg Phe Ala Glu Val 420 425 430

Thr Gln Glu Val Glu Val Ala Arg Pro Val Asp Lys Ala Ile Cys Gly 435 440 445

Leu Thr Pro Gly Arg Arg Tyr Arg Asn Gln Pro Arg Gly Pro Val Gly 450 455 460

Asn Glu Pro Leu Val Thr Asp Val Val Leu Gln Ser Phe Pro Pro Leu 465 470 475 480

Pro Ser Cys Glu Ile Leu Asp Ile Asn Asp Glu Gln Thr Leu Pro Arg 485 490 495

Leu Ile Glu Ala Leu Glu Lys Arg His Asn Leu Arg Gln Met Met Ile 500 505 510

Asp Glu Phe Asn Lys Gln Ser Asn Ala Phe Lys Ala Leu Leu Gln Glu
515 520 525

Phe Asp Asn Ala Val Leu Ser Lys Glu Asn His Met Gln Gly Lys Leu 530 535 540

Asn Glu Lys Glu Lys Met Ile Ser Gly Gln Lys Leu Glu Ile Glu Arg 545 550 555

Leu Glu Lys Lys Asn Lys Thr Leu Glu Tyr Lys Ile Glu Ile Leu Glu 565 570 575

Lys Thr Thr Thr Ile Tyr Glu Glu Asp Lys Arg Asn Leu Gln Glu 580 585 590

Leu Glu Thr Gln Asn Gln Lys Leu Gln Arg Gln Phe Ser Asp Lys Arg 595 600 605

Arg Leu Glu Ala Arg Leu Gln Gly Met Val Thr Glu Thr Thr Met Lys 610 615 620

Trp Glu Lys Glu Cys Glu Arg Arg Val Ala Ala Lys Gln Leu Glu Met 625 630 635 640

Gln Asn Lys Leu Trp Val Lys Asp Glu Lys Leu Lys Gln Leu Lys Ala 645 650 655

Ile Val Thr Glu Pro Lys Thr Glu Lys Pro Glu Arg Pro Ser Arg Glu 660 665 670

Arg Asp Arg Glu Lys Val Thr Gln Arg Ser Val Ser Pro Ser Pro Val 675 680 685

Pro Leu Leu Phe Gln Pro Asp Gln Asn Ala Pro Pro Ile Arg Leu Arg 690 695 700

His Arg Arg Ser Arg Ser Ala Gly Asp Arg Trp Val Asp His Lys Pro 705 710 715 720

Ala Ser Asn Met Gln Thr Glu Thr Val Met Gln Pro His Val Pro His 725 730 735

Ala Ile Thr Val Ser Val Ala Asn Glu Lys Ala Leu Ala Lys Cys Glu
740 745 750

Lys Tyr Met Leu Thr His Gln Glu Leu Ala Ser Asp Gly Glu Ile Glu 755 760 765

Thr Lys Leu Ile Lys Gly Asp Ile Tyr Lys Thr Arg Gly Gly Gln
770 775 780

Ser Val Gln Phe Thr Asp Ile Glu Thr Leu Lys Gln Glu Ser Pro Asn 785 790 795 800

Gly Ser Arg Lys Arg Arg Ser Ser Thr Val Ala Pro Ala Gln Pro Asp

805 810 815

Gly Ala Glu Ser Glu Trp Thr Asp Val Glu Thr Arg Cys Ser Val Ala 820 825 830

Val Glu Met Arg Ala Gly Ser Gln Leu Gly Pro Gly Tyr Gln His His 835 $840 \,$ 845

Ala Gln Pro Lys Arg Lys Lys Pro 850 855